



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

CLV

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,622	09/29/2004	Masakatsu Kawakami	Q83855	1024

23373 7590 01/11/2006
SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT PAPER NUMBER

1652

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/509,622	Applicant(s) KAWAKAMI, MASAKATSU	
	Examiner Iqbal Chowdhury, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2, 8 and 9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/29/04; 9/30/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a 371 of PCT/JP03/07148 filed on 9/29/2004.

The preliminary amendment filed on 10/21/2005 amending claims 3, 8 and 9 and canceling claim 1 is acknowledged. Claims 2-10 are pending.

Applicant's election with traverse of Group V, Claims 8 and 9, directed to a method of screening substance capable of inhibiting the polypeptide in the response filed on 10/21/2005 is acknowledged. Claims 2-10 are pending and are present for examination.

The traversal is on the ground(s) that according to the National Stage Application rule, product, process of making product and process of using product should be examined together, which are not persuasive. In the National Stage application, if product is known then product lacks special technical feature of the invention and there is no contribution over the prior art. Therefore, applicants above mentioned argument does not apply at this situation. As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

However, in response to the applicant's arguments that if the examiner consider to rejoin Group V and Group I or Group V and Group II, applicants would cancel all other pending claims. The examiner finds applicants arguments persuasive because Group V is directed to method of screening compounds capable of modulating the activity of the polypeptide, which belongs to Group I. Therefore; the examiner has agreed to rejoin Group V and Group I. The elected Groups for examination are Group V and I, and thus claims 2 and 8-9 will be examined herein.

Art Unit: 1652

The requirement is still deemed proper and is therefore made **FINAL**.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:

- (1) if a machine or apparatus, its organization and operation;
- (2) if an article, its method of making;
- (3) if a chemical compound, its identity and use;
- (4) if a mixture, its ingredients;
- (5) if a process, the steps.

In this case abstract has two paragraphs. Appropriate corrections are required.

Art Unit: 1652

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 2 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

In the absence of the hand of man, naturally occurring nucleic acids and /or proteins are considered non-statutory subject matter. *Diamond and Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as “An isolated and purified protein or nucleic acid”. For examination purpose the claim is read as such.

Claim Objections

Claims 2, 9 and 10 are objected to because of the following informalities: “amino acid sequence represented by SEQ ID NO: 2” should be “amino acid sequence of SEQ ID NO: 2”. Appropriate corrections are required.

Claim 9 is objected to because of the following informalities: “ostcoarthritis” should be “osteoarthritis”. Appropriate correction is required.

Claims 8 and 9 are objected to as the recitation “95% or more of homology” is grammatically incorrect “ greater than 95% homology” is suggested. Appropriate corrections are required.

Claim 9 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from other claims in the alternative only. Currently, claim 9 depends from both claims 8 and 2 simultaneously. See MPEP § 608.01(n). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8 and 9 are indefinite in the recitation “analyzing whether or not activity” which is indefinite. What activity does it mean?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to use of a genus of protein molecule expressed specifically in RA patients having 95% or more homology to SEQ ID NO: 2. The specification teaches the structure and function of only a single representative species of such proteins and does not contain any disclosure of the structure and function of all protein sequences expressed specifically in RA patients that are 95% identical to SEQ ID NO: 2. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the expression of said polypeptides in RA patients. The genus of protein, having 95%

Art Unit: 1652

identity to SEQ ID NO: 2 is a large variable genus with the potentiality of encoding many different proteins and the specification fails to teach which if any of these beyond SEQ ID NO: 2 are expressed in RA patients and fails to show that, all such proteins are functionally similar to SEQ ID NO: 2 as well. Therefore, many structurally and functionally unrelated polypeptides are encompassed within the scope of these claims. Given this lack of description of representative species and functions encompassed by the methods of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO: 2 and methods for screening for compounds which inhibit the activity of said polypeptide, does not reasonably provide enablement for use of any polypeptide expressed specifically in RA patients and having 95% or more of homology to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 8 and 9 are so broad as to encompass methods for screening for compounds which inhibit the polypeptide of SEQ ID NO: 2 expressed specifically in RA patients and having 95% or more of homology to SEQ ID NO: 2. The scope of the methods claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the method claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which

Art Unit: 1652

changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only one polypeptide for use in the methods claimed.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant method claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the method claims which use any polypeptide with 95% or more homology to the enzymes of SEQ ID NOS: 2 specifically expressed in RA patients because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polypeptide activity; (B) the general tolerance of polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any polypeptide residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of using any polypeptide specifically expressed in RA patients with 95% or more homology to the enzymes of SEQ ID NOS: 2 and an enormous number of amino acid modifications of the enzyme of SEQ ID NOS: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides for use in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Banfi et al. (GenBank Accession No. AF166328, "Homo sapiens NADPH oxidase homolog 1 long form variant (NOH1) mRNA, alternatively spliced, complete cds" and "A mammalian H⁺ channel generated through alternative splicing of the NADPH oxidase homolog NOH-1", Science. 2000 Jan 7; 287(5450): 138-42, see IDS). Banfi et al. disclose the sequence of a human protein NADPH oxidase homolog NOH1, which is 100% homologous to SEQ ID NO: 2 of the instant application. Banfi et al. also disclose the involvement of the NOH1 in voltage-gated proton (H⁺)

Art Unit: 1652

channels in many human and animal tissues and may play an important role in cellular defense against acidic stress.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Banfi et al. (GenBank Accession No. AF166328, "Homo sapiens NADPH oxidase homolog 1 long form

Art Unit: 1652

variant (NOH1) mRNA, alternatively spliced, complete cds” and “A mammalian H⁺ channel generated through alternative splicing of the NADPH oxidase homolog NOH-1”, Science. 2000 Jan 7; 287(5450): 138-42, see IDS) in view of Ostrakhovitch et al. (Oxidative stress in rheumatoid arthritis leukocytes: suppression by rutin and other antioxidants and chelators”, Biochem Pharmacol. 2001 Sep 15; 62(6): 743-6, see IDS). Banfi et al. disclose the sequence of a human protein NADPH oxidase homolog NOH1, which is 100% homologous to SEQ ID NO: 2 of the instant application. Banfi et al. also disclose the involvement of the NOH1 in voltage-gated proton (H⁺) channels in many human and animal tissues and that this protein may play an important role in cellular defense against acidic stress. Banfi et al. does not teach a method of screening substance or compound, which inhibits NADPH oxidase or does not disclose any inhibitors of NADPH oxidase, which might be used for the treatment of rheumatoid arthritis. Ostrakhovitch et al. teach oxidative stress in rheumatoid arthritis leukocytes, which develops due to the activation of NADPH oxidase followed by the accumulation of reactive oxygen species (ROS). Ostrakhovitch et al. also teach a method of identifying compounds, which inhibits oxidative stress and identified rutin, which is very effective against oxidative stress due to the rheumatoid arthritis.

Therefore, it would have been obvious to one of ordinary skill in the art to use the polypeptide of Banfi et al. in the method of Ostrakhovitch to identify or screen compounds or substances for the treatment of rheumatoid arthritis or osteoarthritis.

Conclusion

Status of the claims:

Claims 2 and 8-9 are pending.

Art Unit: 1652

Claims 2 and 8-9 are rejected.

No claim is in condition for allowance.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Iqbal Chowdhury, PhD
Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Remsen Bldg. Rm. 2B69, Mail Box. 2C70
Ph. (571)-272-8137
Fax. (571)-273-8137
IC


REBECCA E. PROUTY
PRIMARY EXAMINER
GICP-1999
1652